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*****CHEMICAL AND PHARMACEUTICAL BULLETIN*****

Yoshikawa M Matsuda H Shimoda H Shimada H Harada E Naitoh Y Miki A
Yamahara J Murakami N

Development of bioactive functions in hydrangeae dulcis folium. V. On the
antiallergic and antimicrobial principles of hydrangeae dulcis folium. (2).
Thunberginol C, D, and E, thunberginol G 3'-O- glucoside, (-)-hydrangenol
4'-O-glucoside, and (+)-hydrangenol 4'-O- glucoside.

In: Chem Pharm Bull (Tokyo) (1996 Aug) 44(8):1440-7

ISSN: 0009-2363

Following the characterization of thunberginols A, B, and F, six bioactive
principles, thunberginols C, D, and E, thunberginol G 3'-O- glucoside,
(-)-hydrangenol 4'-O-glucoside, and (+)-hydrangenol 4'-O- glucoside, were
isolated from Hydrangeae Dulcis Folium, the processed leaves of Hydrangea
macrophylla SERINGE var. thunbergii MAKINO, together with four kaempferol and
quercetin oligoglycosides. Their chemical structures have been determined on the
basis of chemical and physicochemical evidence. Thunberginols C, D, E, and G and
(-)-hydrangenol 4'-O-glucoside showed antiallergic activity in the in vitro
bioassay using the Schultz-Dale reaction. These components also exhibited
inhibitory activities on the histamine release from rat mast cells and on the
histamine-induced contraction in isolated guinea pig tracheal chain. In
addition, thunberginols C, D, E, and G showed antimicrobial activities against
oral bacteria.

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Yoshikawa M Shimada H Yagi N Murakami N Shimoda H Yamahara J Matsuda H
Development of bioactive functions in hydrangeae dulcis folium. VI. Syntheses of
thunberginols A and F and their 3'-deoxy-derivatives using regiospecific
lactonization of stilbene carboxylic acid: structures and inhibitory activity on
histamine release of hydramacrophyllols A and B.

In: Chem Pharm Bull (Tokyo) (1996 Oct) 44(10):1890-8

ISSN: 0009-2363

Lactonization reaction of 2-carboxystilbene mediated by copper(II) chloride
proceeded regiospecifically to give the five-membered lactone, while the
bromolactonizations using N-bromosuccinimide and anodic oxidation were found to
furnish the six-membered lactone. Using these regiospecific lactonization
reactions as a key step, antiallergic and antimicrobial isocoumarins and the
benzylidenephthalides thunberginols A and F and their 3'-deoxyanalogs were
synthesized from phyllodulcin and hydrangenol. Two phthalides called
hydramacrophyllols A and B were isolated from Hydrangeae Dulcis Folium and their
stereostructures were determined on the basis of physicochemical and chemical
evidence, which included the syntheses of hydramacrophyllols A and B from
hydrangenol by the application of the lactonization method using copper(II)
chloride. In addition, hydramacrophyllols A and B were found to exhibit an
inhibitory effect on the histamine release from rat peritoneal exudate cells
induced by antigen-antibody reaction.

Registry Numbers:

147666-80-6 (thunberginol A)

147666-81-7 (thunberginol B)

53902-12-8 (tranilast)

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Yoshikawa M Harada E Naitoh Y Inoue K Matsuda H Shimoda H Yamahara J
Murakami N

Development of bioactive functions in hydrangeae dulcis folium. III. On the
antiallergic and antimicrobial principles of hydrangeae dulcis folium. (1).
Thunberginols A, B, and F.

In: Chem Pharm Bull (Tokyo) (1994 Nov) 42(11):2225-30

ISSN: 0009-2363

From the less polar fraction of *Hydrangeae Dulcis Folium*, the fermented and dried leaves of *Hydrangea macrophylla* Seringe var. *thunbergii* Makino, Eight antiallergic and antimicrobial principles were isolated together with several known compounds. Among the newly isolated bioactive constituents, the chemical structures of thunberginols A, B, and F have been determined on the basis of chemical and physicochemical evidence. Thunberginols A, B, and F were found to exhibit more potent antiallergic activity than phyllodulcin, hydrangenol, disodium cromoglycate (DSCG), and tranilast. In addition, these thunberginols showed antimicrobial activity against oral bacteria.

Registry Numbers:

147666-80-6 (thunberginol A)
147666-81-7 (thunberginol B)
147666-82-8 (thunberginol F)

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Yoshikawa M Ueda T Matsuda H Yamahara J Murakami N
Absolute stereostructures of hydramacrosides A and B, new bioactive secoiridoid glucoside complexes from the leaves of *Hydrangea macrophylla* Seringe var. *thunbergii* Makino.

In: Chem Pharm Bull (Tokyo) (1994 Aug) 42(8):1691-3
ISSN: 0009-2363

Two new bioactive secoiridoid glucoside complexes named hydramacrosides A and B were isolated from the leaves of *Hydrangea macrophylla* SERINGE var. *thunbergii* MAKINO. The absolute stereostructures of hydramacrosides A and B were elucidated on the basis of chemical and physicochemical evidence which included the application of the ¹³C NMR glycosylation shift rule of 1, 1'- disaccharides and the modified Mosher's method. Hydramacrosides A and B exhibited inhibitory effect on the histamine release from rat mast cells induced by antigen-antibody reaction.

Registry Numbers:

50-99-7 (Glucose)

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Yoshikawa M Uchida E Chatani N Kobayashi H Naitoh Y Okuno Y Matsuda H Yamahara J Murakami N
Thunberginols C, D, and E, new antiallergic and antimicrobial dihydroisocoumarins, and thunberginol G 3'-O-glucoside and (-)-hydrangenol 4'-O-glucoside, new dihydroisocoumarin glycosides, from *Hydrangeae Dulcis Folium*.

In: Chem Pharm Bull (Tokyo) (1992 Dec) 40(12):3352-4
ISSN: 0009-2363

New antiallergic and antimicrobial dihydroisocoumarins, thunberginols C, D, and E, were isolated from *Hydrangeae Dulcis Folium*, the fermented and dried leaves of *Hydrangea macrophylla* SERINGE var. *thunbergii* MAKINO, together with new dihydroisocoumarin glycosides, thunberginol G 3'-O-glucoside and (-)-hydrangenol 4'-O-glucoside. Their chemical structures have been determined on the basis of chemical and physicochemical evidence. Thunberginols C, D, E, G, and (-)-hydrangenol 4'-O-glucoside showed antiallergic activity in the in vitro bioassay using the Schults-Dale reaction in sensitized guinea pig bronchial muscle, and they also exhibited antimicrobial activity against oral bacteria.

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Yoshikawa M Uchida E Chatani N Murakami N Yamahara J
Thunberginols A, B, and F, new antiallergic and antimicrobial principles from *hydrangeae dulcis folium*.

In: Chem Pharm Bull (Tokyo) (1992 Nov) 40(11):3121-3
ISSN: 0009-2363

Six new antiallergic and antimicrobial principles, thunberginols A, B, C, D, E, and F, were isolated from *Hydrangeae Dulcis Folium*, the fermented and dried leaves of *Hydrangea macrophylla* SERINGE var. *thunbergii* MAKINO. The chemical structures of thunberginols A, B, and F have been determined on the basis of chemical and physiocochemical evidence. Thunberginols A, B, and F showed more potent antiallergic activity than phyllo dulcin, hydrangenol, and AA-861 in the in vitro test using the Schults-Dale reaction in sensitized guinea pig bronchial muscle. Thunberginols A, B, and F also exhibited antimicrobial activity against oral bacteria.

Registry Numbers:

147666-80-6 (thunberginol A)
147666-81-7 (thunberginol B)
147666-82-8 (thunberginol F)
480-46-6 (phyllo dulcin)
480-47-7 (hydrangenol)
80809-81-0 (AA 861)

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*****JOURNAL OF PROSTHETIC DENTISTRY*****

Nakamoto K Sadamori S Hamada T
Effects of crude drugs and berberine hydrochloride on the activities of fungi.
In: J Prosthet Dent (1990 Dec) 64(6):691-4
ISSN: 0022-3913

The effects of crude drugs on fungi have been used for a thousand years in China and Japan. These drugs include: *Saussureae radix*, *Magnoliae cortex*, *Cinnamomi cortex*, *Hydrangeae dulcis folium*, and *Artemisiae capillarius flos*. The activity of *Coptidis rhizoma* and *Phellodendri cortex* was stronger than other crude drugs against the three fungi. Berberine hydrochloride, which is a component of the two crude drugs, was investigated. Minimal inhibitory concentration values of berberine hydrochloride were 1, 0.125, and 0.5 mg/ml against *Candida albicans*, *C. tropicalis*, and *C. glabrata*, respectively. In *C. glabrata*, compared with *C. albicans* and *C. tropicalis*, berberine hydrochloride greatly inhibited the growth of fungi.

Registry Numbers:

110-54-3 (n-hexane)
2086-83-1 (Berberine)
7732-18-5 (Water)

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*****PLANTA MEDICA*****

Kinoshita K Morikawa K Fujita M Natori S
Inhibitory effects of plant secondary metabolites on cytotoxic activity of polymorphonuclear leucocytes.
In: Planta Med (1992 Apr) 58(2):137-45
ISSN: 0032-0943

The inhibitory effects of 151 natural products, representing most of the frequently occurring types, on the cytotoxicity to MM2 tumor cells of polymorphonuclear leucocytes (PMN) induced by TAK, a polysaccharide immunomodulator, were examined. Forty-two compounds inhibited the TAK-induced activation of PMN. Among them, some naturally occurring quinones and various alkaloids (nicotine, *Cinchona* alkaloids, isoquinoline alkaloids such as cepharanthine, and indole alkaloids such as ajmaline) exhibited potent inhibitory effects. Using the inhibition assay for monitoring, the extracts of *Hydrangea Dulcis folium*, *Scopoliae rhizoma*, *Cinchona cortex*, *Magnoliae cortex*, *Stephania tuber*, and *Rauwolfia radix* were analysed to characterize the active constituents.

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*****YAKUGAKU ZASSHI. JOURNAL OF THE PHARMACEUTICAL SOCIETY OF JAPAN*****

Yamahara J Matsuda H Shimoda H Ishikawa H Kawamori S Wariishi N Harada E
Murakami N Yoshikawa M

[Development of bioactive functions in hydrangeae dulcis folium. II. Antiulcer,
antiallergy, and cholagoic effects of the extract from hydrangeae dulcis folium]

In: Yakugaku Zasshi (1994 Jun) 114(6):401-13

ISSN: 0031-6903 (Published in Japanese)

In order to develop new bioactive functions of Hydrangeae Dulcis Folium, the
fermented and dried leaves of Hydrangea macrophylla Seringe var. thunbergii
Makino, effects of the methanolic extract from the crude drug on antiulcer,
antiallergic, cholagoic, and various pharmacological actions were investigated.
Consequently, the methanolic extract was found to exhibit potent antiulcer,
antiallergic, and cholagoic activities. By monitoring with these activities, it
was found that the active constituents were contained in the lipophilic portion
of the methanolic extract. Furthermore, the known lipophilic constituents such
as phyllodulcin and hydrangenol were found to show little antiulcer and
cholagoic activities, while it was also found that they showed antiallergic
activity on Schultz-Dale reactions.

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Yoshikawa M Chatani N Harada E Nishino Y Yamahara J Murakami N
[Quantitative analysis of dihydroisocoumarin constituents of Hydrangeae Dulcis
Folium by means of high performance liquid chromatography. Chemical
characterization of the processing, distribution in plant, and seasonal
fluctuation]

In: Yakugaku Zasshi (1994 Mar) 114(3):176-81

ISSN: 0031-6903 (Published in Japanese)

In order to characterize the chemical change of the constituents during the
processing of Hydrangeae Dulcis Folium, quantitative analyses of phyllodulcin,
hydrangenol, and their 8-O-glucosides were developed by means of high
performance liquid chromatography. As an application of this HPLC method, the
distribution of those dihydroisocoumarins in different parts of Hydrangea
macrophylla var. thunbergii was investigated. It was found that these
dihydroisocoumarins were contained at the highest concentration in the leaves.
Furthermore, the seasonal fluctuation of these compounds in the leaves, together
with the height of the plant and total dry weight of the leaves, were clarified
and so that the suitable period for the harvest of Hydrangea macrophylla var.
thunbergii was deduced to be from Oct. to Nov.

Registry Numbers:

480-46-6 (phyllodulcin)

480-47-7 (hydrangenol)

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[illegible]

Development of bioactive functions in hydrangeae dulcis folium. V. On the antiallergic and antimicrobial principles of hydrangeae dulcis folium. (2). Thunberginols C, D, and E, thunberginol G 3'-O- glucoside, (-)-hydrangenol 4'-o-glucoside, and (+)-hydrangenol 4'-O- glucoside.
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480-47-7 (hydrangenol)

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